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The goal of the research effort funded under this grant is to finalize the construction of two prototype DXM-1 slot-scanning digital mammography systems, conduct a technical evaluation of these prototypes and perform two clinical studies to assess the efficacy of the systems in the clinical environment. The technical evaluation and one of the clinical studies is being conducted at the Radiology Department at the University of Arizona (UA). The objective of the technical evaluation is to determine system performance parameters such as dynamic range, modulation transfer function, sensitivity, etc. The second clinical study is scheduled to be conducted at the Radiology Department at the University of California at San Diego (UCSD) and will establish the clinical efficacy of the system compared with conventional film/screen mammography. One thousand women are scheduled to participate. Construction of the prototypes is essentially complete, technical evaluation is partially complete and the clinical studies are scheduled to begin in October, 1998. Preliminary data gathered indicates that image quality parameters of the DXM-1 system are superior to film/screen mammography and can be obtained with lower patient dose.

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PI - Signature FOR   9/29/98
RONALD B. SCHILLING   Date

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INTRODUCTION

The goal of the research effort funded under this grant is to finalize the construction of two prototype DXM-1 slot-scanning digital mammography systems[1], conduct a technical evaluation of these prototypes and perform two clinical studies to assess the efficacy of the systems in the clinical environment. This program is scheduled to be completed during a 36-month effort.

The technical evaluation and one of the clinical studies is being conducted at the Radiology Department at the University of Arizona (UA) under the direction of Dr. Hans Roehrig. The objective of the technical evaluation is to determine system performance parameters such as dynamic range, modulation transfer function, sensitivity, etc. These parameters are to be measured and compared with film/screen performance characteristics. The objective of the clinical study conducted at UA is to acquaint and train radiologist to read digital mammograms from a monitor and to determine system efficacy in screening and diagnosis by imaging patients with known abnormal mammograms. One hundred women are scheduled to participate in this study.

The second clinical study was scheduled to be conducted at Sharp Healthcare/Sidney Kimmel Cancer Center in San Diego, California under the direction of Dr. Christine White. The objective of this study is to establish the clinical efficacy of the system compared with conventional film/screen mammography. One thousand women are scheduled to participate in this study.

The DXM-1 digital mammography system was designed and partially developed through funding obtained from the National Institutes of Health with two Small Business Innovative Research (SBIR) grants (phase I and phase II grant no. 2R44CA59104-02AI). Under these grants, the sensor chip technology was developed and an engineering prototype was produced which was used to acquire images of the Contrast Detail Mammography (CDMAM) phantom. These images established that the sensors are capable of acquiring superior quality images than conventional screen/film. Data acquired from these images was used to calculate the Detective Quantum Efficiency (DQE) and Modulation Transfer Function (MTF) for the prototype sensor array and is shown in Appendix A.

One result of the previous work was that it was determined that the original prototype sensors were not optimum for use in full-field mammography applications. A new sensor was designed incorporating several features including larger pixel size, larger active area on the sensor (i.e., more pixels) and an on-chip Time Delay and Integration (TDI) function. A camera and digital signal processor (DSP) was also designed during this effort.

Fisher Imaging Corporation, a subcontractor to this effort had previously developed a mammography gantry specifically designed for use with a digital slot-scanning imaging system using a different sensor technology. In connection with this effort Fisher has delivered two prototype gantries for use in the technical and clinical evaluation studies.

The effort described above is broken down into three tasks: Integrate and Optimize the DXM-I Mammography System, Engineering and Technical Evaluation; and Clinical Studies. The progressmade during this reporting period for each of these tasks is discussed below.

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TASK 1: DXM-1 Mammography System Integration

This task, scheduled to require nine months to complete has been delayed due to the necessity of redesigning the sensor chip and additional modifications required to the DSP unit. The sensor chips used in the DXM-1 were designed and fabricated in connection with previous work and were tested last year. The results obtained indicated that resolution was being degraded in the in-scan axis of the image. After subsequent analysis, it was determined that the chip design allowed for parasitic capacitance or charge sharing among the TDI summing capacitors on the sensor readout chip. In addition, the sensors produced in that lot run had an extremely low yield such that only 2 working sensor were produced.

To correct these problems, the sensor chip was redesigned, a new mask set was generated and another lot run was initiated. This lot run produced poor results and a meeting with the wafer fabrication vendor (Orbit Semiconductor, Sunnyvale, CA) was held. The source of the problems resulting in poor yield was not established. The lot runs fabricated to that point were made on Orbit's 4-inch wafer fab line which was in the process of being phased out. Orbit has set up a 6-inch wafer fab line and they agreed to re-run the lot on the new line. A new mask set was made to adapt to the 6-inch format and a lot run was made. The yield on the new lot run was significantly improved and many working chips were produced. A photograph of an assembled and packaged sensor is shown in Figure B1.

The 2-channel DSP unit required several modifications in order to operate at the desired speed (i.e., 10 MHz) using a software-implemented image formation algorithm. Since this has now been accomplished, two 8-channel DSP units are being fabricated that utilize a firmware implemented image formation algorithm that will run at a speed of (20 MHz). This higher operating speed is required in order to meet the goal of acquiring a full-field mammographic image in four seconds.

The contractor that was chosen to design and fabricate the DSP units is Berkeley Camera Engineering, Inc. They designed, fabricated and delivered the 2-channel DSP unit during the previous reporting period. Efforts to produce a fully functional 8-channel DSP unit have not met with success. Berkeley Camera Engineering is still working on the problem and has recently delivered an 8-channel DSP unit that only works at 8 MHz. The DSP unit was scheduled to be delivered 1 year ago and function at 20 MHz. This has caused additional delays in getting the DXM-1 system integrated and the subsequent technical and clinical evaluation tasks.

Fischer Imaging Corporation has delivered the second Senoscan mammography gantry that is to be used for the technical and clinical evaluation tasks. The gantry and its SUN workstation was modified to accommodate and operate the DXM-1 imaging system. Figure B2 shows the assembled detector module with its eight sensor chips. Underneath the sensors are two printed circuit boards containing the analog signal processor where the sensor output is digitized and sent to the DSP unit. Figures B3 and B4 show the Senoscan unit with the generator housing removed. In these two views, the generator and collimator are exposed. Figures B5 and B6 show the gantry fully assembled. Figure B6 shows the gantry next to an engineer to give the reader a perspective on the size of the gantry.

The Fischer x-ray system is constructed with an embedded microprocessor. This embedded processor controls the x-ray generator, a Galil motion controller, and the filter wheel. The x-ray generator, which also has an embedded processor, is connected to the microprocessor through a serial interface. The microprocessor sends commands to the x-ray generator to control tube current, kVp and exposure time. The Galil is a programmable motor controller that controls the rotation, elevation, breast compression plate and scan arm motion. The Galil is connected to the microprocessor through a custom parallel interface. The microprocessor sends commands to the Galil to adjust elevation, rotation, and compression, and to initiate and control the scan velocity. The Galil sends position information to the microprocessor from a rotation sensor and a compression thickness sensor. The filter wheel assembly has it's own controller connected to the microprocessor through a serial interface. The microprocessor sends commands to the filter controller to select one of three different filters. Currently the filters available are rhodium, molybdenum and aluminum.

Fischer Imaging has provided a custom microprocessor configuration with a programmable tube current, kVp, x-ray exposure time, filter position, and scan velocity, with a dumb terminal over a serial interface. Compression thickness, rotation position and other system status codes are accessable through the serial interface as well. A foot pedal and a manual knob, located on the x-ray system, controls compression. Thumb switches, also located on the x-ray system, control rotation and elevation. X-ray and scan initiation is controlled by a standard dead-man switch configuration.

Software for a graphic user interface (GUI) has been written that allows the operator of the system to enter the desired x-ray technique parameters from the host computer, currently a Sun Ultra 10 workstation. This GUI sends the proper ASCII commands to the microprocessor emulating a dumb terminal output and receives and displays the technique parameters.

A safety interlock has been designed and built that consists of an interlock board that plugs into the parallel port of the host computer. The host computer sends a heartbeat signal to the interlock board. The heartbeat signal consists of two, eight bit words that alternate at one-second intervals. The heartbeat signal is sent to the interlock board only if the technique parameters received by the host computer match the parameters entered by the operator. The host computer monitors the x-ray tube heat loading and will disrupt the heartbeat signal if the tube heat loading exceeds specifications. If the heartbeat signal is not present, the interlock board disconnects power to the dead-man switch on the x-ray system, disabling x-ray initiation. The heart beat signal provides an intrinsically safe interlock for such things as computer glitches and unauthorized access.

An image restoration program has also been written to stitch together the 16 individual image strips acquired (one for each of 2 banks of pixels on each of the 4 sensors). The assembled image is formatted for storage using a file format compatible with any of several image processing programs that will permit the radiologist to enhance, display, archive or print the acquired image. The GUI program described above will permit the radiologist to control the operating parameters of the mammography gantry and acquire images.

At this time the entire system has been fully integrated albiet with a DSP unit that works at 8 MHz instead of the specified 20 MHz.

TASK 2: Engineering and Technical Evaluation of the DXM-1 System

Several images were acquired during the previous reporting period with the first prototype using only two of the required eight sensor chips. Although this system has only 1/4 of the total imaging area, several images were acquired and were analyzed. The data so produced has been used to complete the development of the system and make the required changes to the sensor chips and DSP unit. These images have been printed on a laser film printer and photographed with a Minolta digital still camera. The digital images were imported into Adobe Photoshop where some contrast enhancements and cropping was performed. These images were then printed on an inkjet printer with 300 dots-per-inch resolution. Figure B7 shows a photograph of the prototype 2-channel imaging system. As shown the gantry is a simplified version of the Senoscan unit and contains a lower power x-ray generator. The SUN workstation and DSP unit used to acquire images is shown in Figure B8. As shown the DSP unit is connected to the analog signal processor by several ribbon cables. Images are acquired and displayed on the SUN workstation.

Figure B9 shows an image acquired of a cadaver breast imbedded in wax. This image was acquired with 10 line-pairs-per-millimeter (lp/mm) resolution. Figure B10 shows and enlarged portion of the cadaver breast where some micro-calcifications have simulated by placing ground up oyster shells into the breast tissue. As shown the particles are easily visible and can be seen in the upper central portion of the image. It should be noted here that the steps taken to reproduce these images for this report have significantly reduced the quality of the acquired images and consequently, the quality of these images cannot be fully appreciated here.

Figure B11 shows an image acquired of the American College of Radiology (ACR) Accreditation Phantom. The ACR accreditation phantom is described in detail by DeParedes, et al[2], Hendrick, et al[3], and McLelland, et al[4]. Figure B12 shows the same phantom imaged with traditional film/screen techniques. A schematic of the accreditation phantom is shown in Figure B13. These images were acquired during the previous reporting period but were not available in time for publication. To review, images of the phantom acquired with the DXM-1 prototype at an exposure of 75 mAs, mass groups 13 - 15 were visible, while 16 was not. Mass group 16 was not visible at an exposure of 100 mAs. These images were produced with a dark-subtraction and flat-fielding algorithm applied to the raw image data.

Figure B14 shows an image acquired of the CDMAM phantom. As shown the phantom consists of a gold foil containing a grid. Each square in the grid contains two gold disks of varying thickness and diameter. One of the disks is placed in the center of each square with the second disk placed in one of the four corners in a random pattern. Figure B15 shows a small area of interest of this image. A portion of the phantom is shown with disks that are barely resolvable with the DXM-1 prototype. The disks imaged here indicate that the DXM-1 prototype has excellent contrast resolution. These disks are the smallest in the grid indicating that 100% of the disks are visible. By comparison, a typical mammographic stereotatic biopsy system using a CCD camera can only see about 50 - 60% of these disks.

A major part of the work during this reporting period at the University of Arizona was devoted to the development of software necessary to do image analysis. This development became

desirable and even necessary since the Dept. Radiology at the University of Arizona decided to replace their "main-frame" computer VAX 8300 by high-performance PCs operated under Windows 95 or Windows NT operating systems. In addition, no image analysis software was available at Primex General Imaging Corp.(PGI), therefore this software development was particularly important permitting image analysis directly at PGI facilities.

The basis for this software development is the Interactive Data Language Version 5.1. This IDL (Interactive Data Language) is a complete computing environment for the interactive analysis and visualization of data. IDL integrates a powerful, array-oriented language with numerous mathematical analysis and graphical display techniques. Programming in IDL is a time-saving alternative to programming in FORTRAN or C-using IDL, tasks which require days or weeks of programming with traditional languages can be accomplished in hours. Users can explore data interactively using IDL commands and then create complete applications by writing IDL programs.

Advantages of IDL include:

- IDL is a complete, structured language that can be used both interactively and to create sophisticated functions, procedures, and applications.

- Operators and functions work on entire arrays (without using loops), simplifying interactive analysis and reducing programming time.

- Immediate compilation and execution of IDL commands provides instant feedback and "hands-on" interaction.

- Rapid 2-D plotting, multi-dimensional plotting, volume visualization, image display, and animation allow you to observe the results of your computations immediately.

- Many numerical and statistical analysis routines-including Numerical Recipes routines-are provided for analysis and simulation of data.

- IDL's flexible input/output facilities allow you to read any type of custom data format. Support is also provided for common image standards.

- IDL widgets can be used to quickly create multi-platform graphical user interfaces to your IDL programs.

- IDL programs run the same across all supported platforms (Unix, VMS, Microsoft Windows, and Macintosh systems) with little or no modification. This application portability allows you to easily support a variety of computers.

- Existing FORTRAN and C routines can be dynamically-linked into IDL to add specialized functionality. Alternatively, C and FORTRAN programs can call IDL routines as a subroutine library or display "engine".

This IDL Interactive Data Language permitted us to develop software for a variety of image analysis tasks, some of which are described in the following. The basic approach follows the concepts of image analysis as discussed in the classic text by Dainty and Shaw [5] and selected other papers like Fujita [6] and Hillen [7].

A. Determination of image statistics

Here a region of interest within the image is selected and the software determines the

- mean digital value within this region of interest
- standard deviation
- maximum pixel value
- minimum pixel value

B. Performing 1-D and 2-D Fourier Transforms

Such Fourier Transforms are required if one wants to determine the Noise Power Spectrum as well as the Modulation Transfer Function. The Fourier Transforms are of the 512 point discrete type.

1. Noise Power Spectrum (NPS).

The Noise Power Spectrum is found basically from the square of the Fourier Transform. Particular features include subtraction of a fixed mean, subtraction of a mean found from a sliding window of selectable size. There is no normalization, i.e. the value is not unity a zero spatial frequencies. The value of the noise power at zero spatial frequency is found from extrapolation of the lowest 5 spatial frequency values to zero spatial frequency.

2. Modulation Transfer Function (MTF)

The basis of MTF measurements are 1-D Fourier Transforms of single-line-profiles i.e. the MTF is found from the Line-Spread-Function. For instance, for finding the MTF of the DXM-1 System, a narrow slit of width about 10 μm width is imaged with the digital system and the resulting image of the slit is subjected to a 1-D Fourier Transform. Unfortunately, due to the fact that the imaging system is digital, the pixel spacing is discrete, and specifically, it is 25 μm. That means the sampling frequency for sampling the image of the slit is not high and cannot get a good resolution for measuring the line-spread-function. This limitation can be overcome by placing the imaging slit under an angle of between 1 and 2 degree with respect to the image lines as shown by Fujita et.al. [6]. Taking adjacent columns, one obtains a series of profiles which correspond to profiles which are shifted by distances of sub-pixel magnitude such that the effective pixel spacing is a fraction of 25 μm and the MTF is measured to much higher resolution than possible without this "trick". The resulting MTF is called the "pre-sampling" MTF. This particular feature of obtaining the pre-sampling MTF is built into the MTF program.

C. Making one-dimensional horizontal or vertical profiles..

Here a region of interest is selected preferably a predominantly one-dimensional one like a narrow horizontal one or a narrow vertical one and then the average pixel values are plotted as a function of position along the long dimension of the Region Of Interest (ROI).

This feature is particularly important to detect any low-spatial frequency non-uniformities (like shading) across the field of view and permits better planning the process of MTF or NPS measurements.

D. Making 2-D plots

Similar to the 1-plots, 2-dimensional plots are useful for detecting any low-spatial frequency non-uniformities (like shading) across the field of view

E. Normalization or flatfielding

A particular problem of digital image detectors is the variation of responsivity or gain from pixel to pixel. Virtually every pixel has a different responsivity. As a result, even if the object to be imaged were very constant, there would be variations in the image which are due to properties of the image detector. Assuming, the imaging detector can be considered a linear system, such variations in responsivity can be eliminated by a process known as flatfielding.

Here a reference image REF(x,y) or flatfield is generated by exposing the imaging system to a uniform radiation field (no object present). In order to eliminate temporal fluctuations not only is one reference image made but at least 10 such reference images and subsequently a temporal average is made by averaging these 10 uniform images to form the reference image REF(x,y).

Similarly a dark image DRK(x,y) is generated, also averaged over at least 10 trials. Then the object to be imaged is placed into the imaging system's field of view and a raw image Raw(x,y) is generated. This raw image is flatfielded or normalized by applying the following procedure:

$$FF(x,y) = ([Raw(x,y) - DRK(x,y)]/[REF(x,y) - DRK(x,y)])*AVE_{REF}$$

where AVE_{REF} is the average value of the reference image REF(x,y) .

F. Contrast Stretching

This feature works simply like window and level, where a look-up table is generated between two buffer memories. The slope determines the contrast and the level determines the off-set values. In addition, the contrast can also be stretched according to the pixel values applying Histogram Equalization.

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G. Binning

The feature of binning is important for the investigation of the necessary spatial resolution for imaging a particular pathology. Like in the case of mammography, it is still not known, which pixel matrix is sufficient for the 8" x 10" format: 8,128 x 10,160 (with a 25 μm spotsize. This would correspond to the MTF and spatial resolution of the conventional film/screen combination) or 4,064 x 5,080 (with a 50 μm spot-size). In order to investigate this problem, the image should be taken at high spatial resolution, say 8,128 x 10,160 pixels and displayed at that spot size. Then the image would be binned, say 2:1. This binning operation would reduce the resolution dependend on the size of the binning. For the case of 2 x 2 binning, four pixels will be replaced by 1 pixel and the resultant image will be 4,064 x 5,080. In the next step one would use 4 x 4 pixel binning, i.e. 16 pixels of the original image will be replaced by 1 pixel and the resultant image will be 2,032 x 2,540 pixel

The binning procedure developed permits binning to more than 10:1

H.　Image Math

Image math permits a variety of mathematical processes to be applied to an image or to several images. Very often one needs to subtract two images; this feature is important when no reference image is available and flatfielding is not possible. At other occasions it is required to multiply an image with a constant or to divide it by a constant; or one needs to add or subtract a constant to or from an image.

I　Image Manipulation

Image manipulation is an important feature when images with different orientation are to be compared. Here rotation, flipping or reversing the signal from positive to negative (reverse video) is often required for optimum comparison.

J.　Time-Delay Integration

Of particular importance to the software development is the feature of simulating time delay integration. A crucial element of the DXM-1 digital mammography system is the time-delay integration, which permits achieving practical acquisition ("scanning") times of about 6 sec. Time-delay integration is discussed by Haus and Yaffe [8]. Time-delay integration provides integration of the x-ray signal as the scanning slot scans across the object. Unfortunately the process of time-delay integration also provides integration over the stationary spatial non-uniformities (like differences in pixel-sensitivities or pixel-defects) which are normally eliminated from the image by the process of flat-fielding.

The combination of time-delay integration and flat-fielding is a major issue and needs to be addressed. In order to address this problem, software was developed to simulate time-delay integration. Here a series of uniform images taken with a CCD based fiber-optically coupled x-ray camera was taken. The resolution of the CCD camera was 1,024 x 1,024. Then

each image was shifted by one column with respect to the previous one and then all images were added and the total sum divided by the number of images taken. For example, if 15 images were taken, the second one would be shifted by 1 column, the third one would be shifted by 2 columns, the fourth one would be shifted by three columns and so on until the fifteenth one, which would be shifted by 14 columns. Assuming, that the CCD camera had 12 bits and each individual image was exposed to a mean value of 3,500 ADU with a standard deviation of 15 ADU. After averaging the mean value in most of the image would be still 3,500 ADU but now the standard deviation would be 3.87.

Experiments were made with such a CCD camera and showed indeed the expected improvements in signal-to-noise ratio. Experiments are still going on to investigate the optimum way to flat-field.

TASK 3: Clinical Studies to Assess Efficacy of the DXM-1 Digital Mammography System

In the previous reporting period, the principal investigator for the clinical trial program subcontracted to Sharp Healthcare, Dr. Christine White, left her position there. One of her colleagues, Dr. Linda Olson is a professor at the University of California at San Diego (UCSD). She has agreed to become the principal investigator for the clinical trial program and run it through the university hospital.

A request for a change of venue was made for the clinical trial program in connection with this effort from Sharp Healthcare to UCSD on June 13, 1997. A reply was received requesting a protocol, IRB approval safety program and patient informed consent form from UCSD, a CV from Dr. Olson and a redirection of funds budget. These items were forwarded to the MCMR grants office on June 30, 1997. Final approval to transfer the clinical trial program to UCSD has since been obtained from the Army.

The revised clinical trial program is proposed to begin on October 15, 1998. The scope of work proposed is essentially identical to the original trial and the proposed budget will not change the current level of funding for this grant. In order to expedite the initiation of the clinical trial program, a small pilot study involving 10 women is scheduled to begin on October 15, 1998. This study will be conducted at PGI laboratory facilities in San Marcos, CA. Data obtained from this study will be used to determine if any modifications are required to the DXM-1 hardware or software configurations before the system is moved to UCSD and the University of Arizona for the planned clinical evaluations.

Conclusions

Overall progress to date on this effort has been delayed due to technical difficulties in the DXM-1 system integration. Moreover, one of the clinical trial venues was changed due to the departure of the program director at the originally chosen facility. This has resulted in a slippage in milestone performance of twelve to eighteen months in some cases. The DXM-1 system integration task is largely complete with the exception of the DSP unit which still does not function at the desired operating speed of 20 MHz. The technical evaluation task is about half way complete. Further

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evaluation studies will be conducted once the DSP is completed and the DXM-1 system is fully integrated.

Progress towards final system integration of the DXM-1 has been hampered by poor performance of the DSP unit. Although a fully functional 10 MHz 2-channel DSP unit has been delivered and was used to obtain data reported in the previous report, the 8-channel DSP unit just delivered can only operate at 8 MHz. This is sufficient to enable us to initiate the clinical studies portion of the effort. However, we believe that 20 MHz operation is required for optimum performance.

Some conclusions can be made at this time based on the preliminary data gathered thus far on the DXM-1 system. The system response is linear with exposure dose and it appears that the dominant noise source is quantum (x-ray) noise. Efforts are now underway to improve system performance by removing artifacts generated in the image reconstruction process and to eliminate parasitic capacitance on the readout IC.

PGI has entered negotiations with another vendor to fabricate a 20-MHz DSP unit. This vendor, InfiMed, Inc. of Liverpool, NY, has agreed to supply the DSP unit and a contract should be issued to InfiMed next month. It is anticipated that a fully functional DSP will be delivered in January, 1999. Due to the interest shown by InfiMed and other medical x-ray imaging companies in this technology, we anticipate that sufficient funds will be invested in this program from commercial sources during the next 12 months to allow us to complete this project, although some delay is anticipated.

During the next reporting period a significant amount of technical and clinical data will be generated in connection with this program. Preliminary findings indicate that the primary objective of this effort, the demonstration of a new imaging technology that has superior performance to conventional film will be established. Of particular importance is the fact that through this program, significant clinical and technical data will be generated that will greatly enhance the viability of this technology and will greatly expedite the transition of this technology into the clinical environment. Thus far we have established that the system performance for mammographic imaging is superior to conventional mammography and to other competing digital technologies now under development. The DXM-1 has a true 50 micron pixel with extrapolation capabilities to 25 micron pixels and can offer this resolution at a low patient dose.

Discussions are underway with Xicon, Inc., a subsidiary of InfiMed, Inc. regarding a collaborative effort to modify PGI's silicon-based hybrid PIN diode sensor. InfiMed is an established manufacturer of digital medical x-ray imaging equipment. This effort contemplates substituting the existing silicon PIN diode structure with a layer of thallium bromide. The existing hybrid PIN doide sensor consists of a Complementary Metal Oxide Semiconductor (CMOS) readout Integrated Circuit (IC) that is connected to a silicon PIN diode array through an array of indium bump bonds. Thallium bromide is a photoconductor material that has excellent x-ray absorption and quantum gain characteristics. Replacing the silicon PIN diode array with a layer of thallium bromide has the potential to dramatically lower the cost of the sensor array and significantly improve its imaging performance characteristics.

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Xicon was awarded an IDEA grant under the U.S. Army Breast Cancer Research Program last year. They proposed to team up with FED Corporation to produce a prototype full-field mammography detector. Apparently, FED Corporation has been unable to deliver their portion of the prototype and the project is at a standstill. A proposal is being prepared to petition the Army to modify the scope of the IDEA grant to apply the photoconductor coating to the slot-scanning sensor under development in this grant. If the proposed effort turns out to be successful, it could have a significant impact on both technologies. Moreover, the development of a successful application method for the thallium bromide photoconductor on the CMOS readout IC would pave the way for an application method on an amorphous flat-panel detector as well. The application of thallium bromide on a flat panel detector would improve the performance of flat panel detectors for full-field mammography applications where scanning is not required.

References

1. Cox, J.D., Sharma, S.R., and Schilling, R.B., "Advanced Digital Mammography", Proceedings of the Annual Meeting of the Society for Computer Applications in Radiology (SCAR), June 21-24, 1997, Rochester Minnesota.

2. DeParedes ES, Frazier AB, Hartwell CD, et al: Development and implementation of a quality assurance program for mammography. Radiology 163:83-85, 1987.

3. Hendrick RE: Standardization of image quality and radiation dose in mammography. Radiology 174:648-654, 1990

4. McLelland R, Hendrick RE, Zinninger MD, Wilcox PA: The American College of Radiology Mammography Accreditation Program" AJR 157:473-479, 1991

5. Dainty, J.C., and R. Shaw, **"Image Science; principles, analysis and evaluation of photographic-type imaging processes"**, Academic Press, London, New York, San Francisco, (1974)

6. Fujita, H., Ueda, K., Morishita, T., and Ohtsuka, A., Basic imaging properties of a computed radiography system with photostimulable phosphors. Med. Phys, 1989. 16, p. 52.

7. Hillen, W., Schiebel, U. and Zaengel, T., Imaging performance evaluation of a digital storage phosphor system. Med. Phys., 1987. 14, p.744.

8. Haus AG, Yaffe MJ, edt: "Syllabus: A Categorical Course in Physics; Technical Aspects of Breast Imaging". Second and updated edition; (1993) RSNA Publications, 2021 Spring Road, Suite 600, Oakbrook, IL 60521

Appendix A

# Primary Slot Scan System DQE is About 10x Better Than Film-screen

- Quantum efficiency of a 1.5mm detector is over 80%.
- Scatter and grid effects reduce system DQE of film-screen to about 7%.
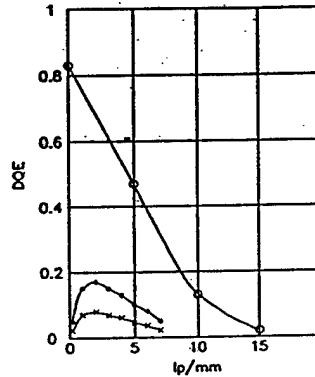
Ref: "Detective quantum efficiency of selected mammographic screen-film combinations." In: Medical Imaging III: Image Formation, SPIE 1090, 1989: p72-74

• — DQE of Kodak MIN-R Screen/Ortho-M Film
o — DQE of 1.5mm Thick PrimeX Detector
x — System DQE of Film/Screen With Scatter Grid

Modulation Transfer Function Data Approaches Predicted Values
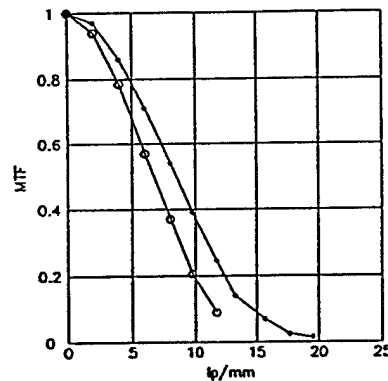
• — MTF of 1mm Detector (2 Samples per Dwell)
o — MTF of 1mm Detector (1 Sample per Dwell)

Experimental DQE Data Consistent With Predictions

o — Measured DQE
• — Predicted DQE (W Target X-ray Spectra)
• — Predicted DQE (Mo Target X-ray Spectra)
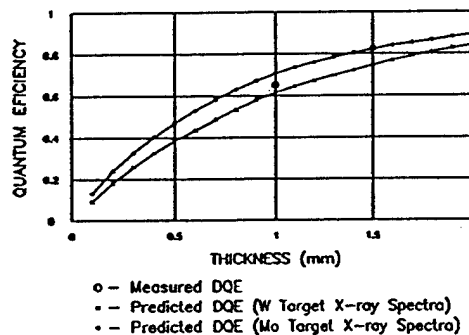
Figure A-1

Appendix B
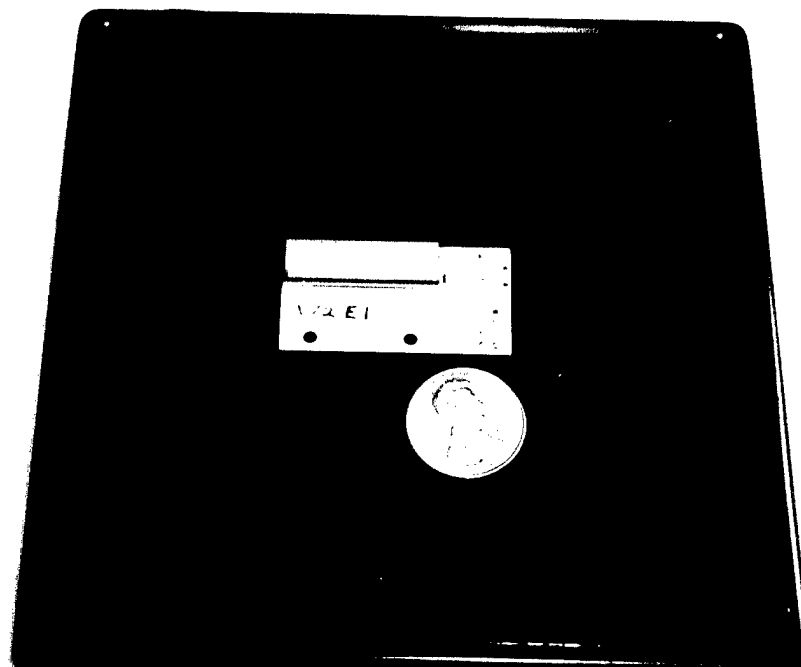
Figure B-1: Silicon-Based Hybrid PIN Diode Array
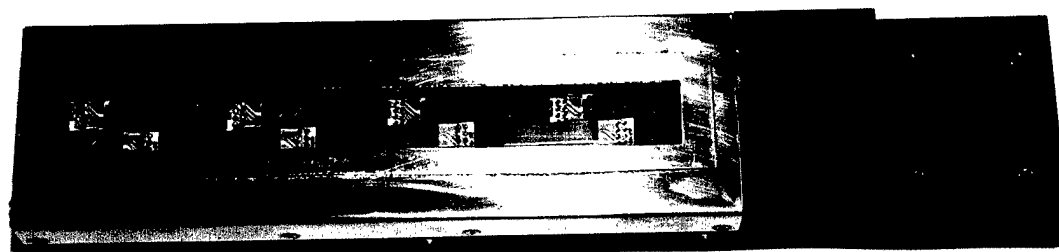
Figure B-2: DXM-1 Detector Module

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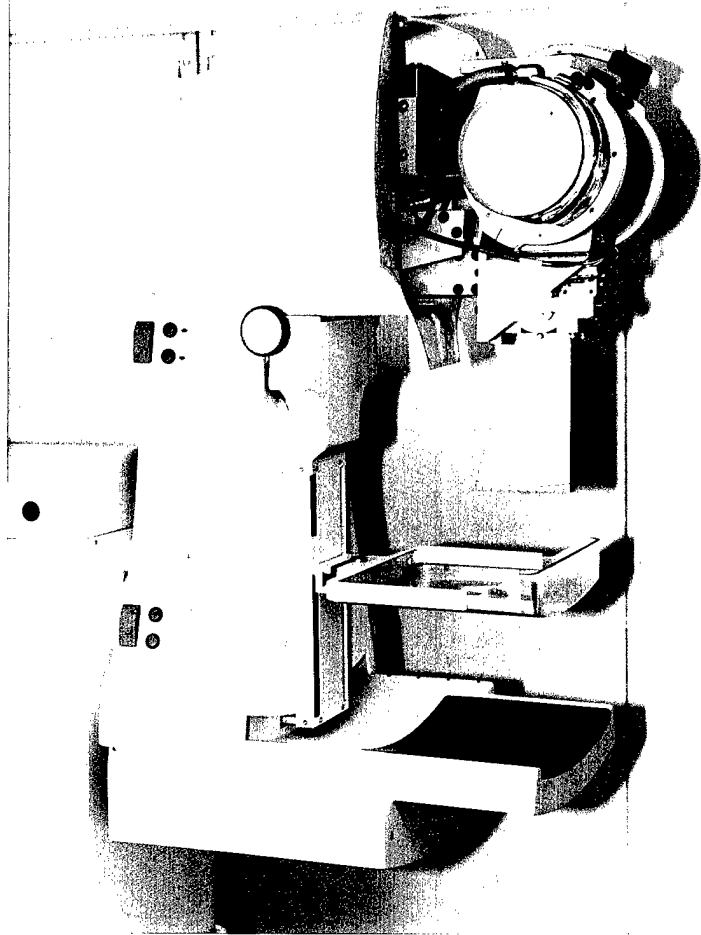
Figure B-3: Fischer Imaging Corporation's Sensoscan
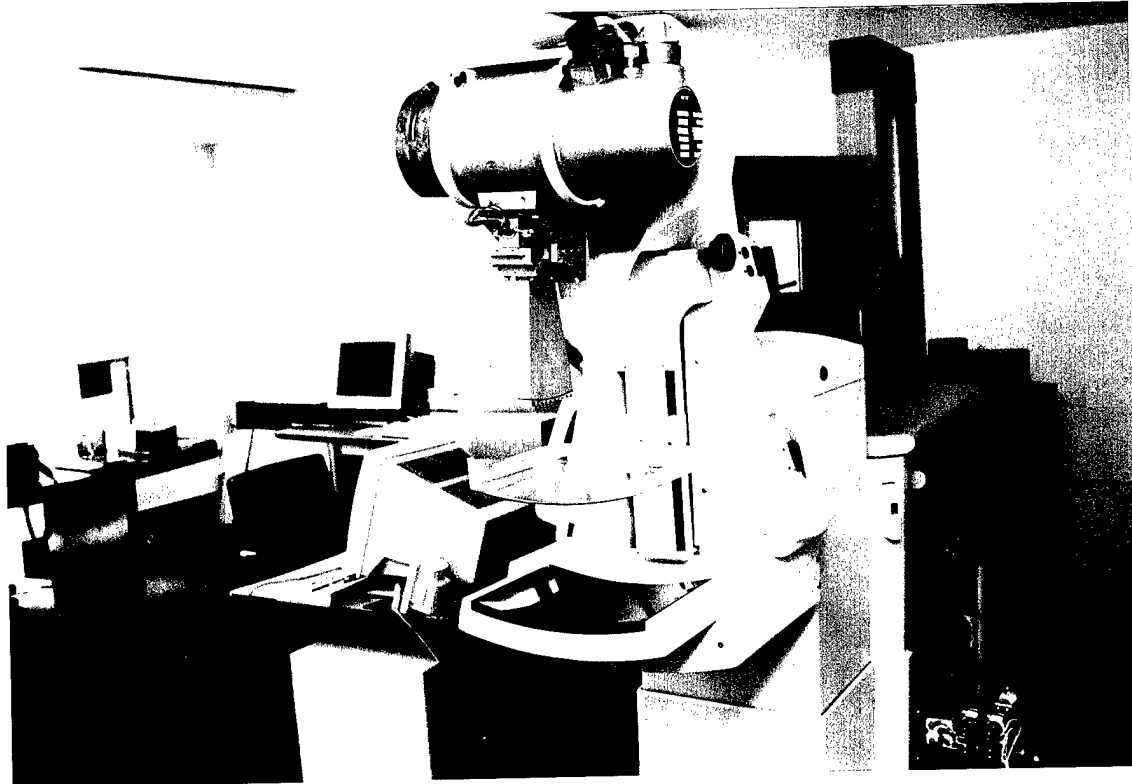Digital Mammography Gantry – Side View
Tube Head Exposed

Figure B-4: Fischer Imaging Corporation's Sensoscan
Digital Mammography Gantry – Front View
Tube Head Exposed

Figure B-5: Fischer Imaging Corporation's
Sensoscan Digital Mammography
Gantry – Front View

Figure B-6: Fischer Imaging Corporation's Sensoscan
Digital Mammography Gantry – Side View
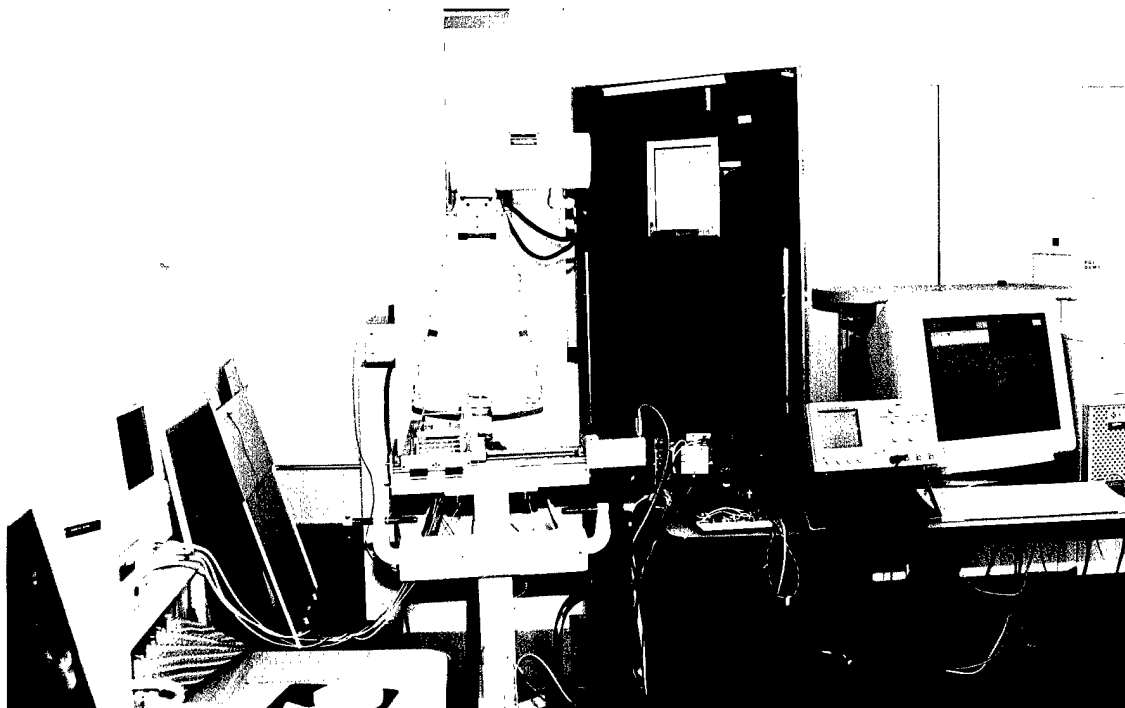
Figure B-7: Prototype 2-channel DXM-1 DSP
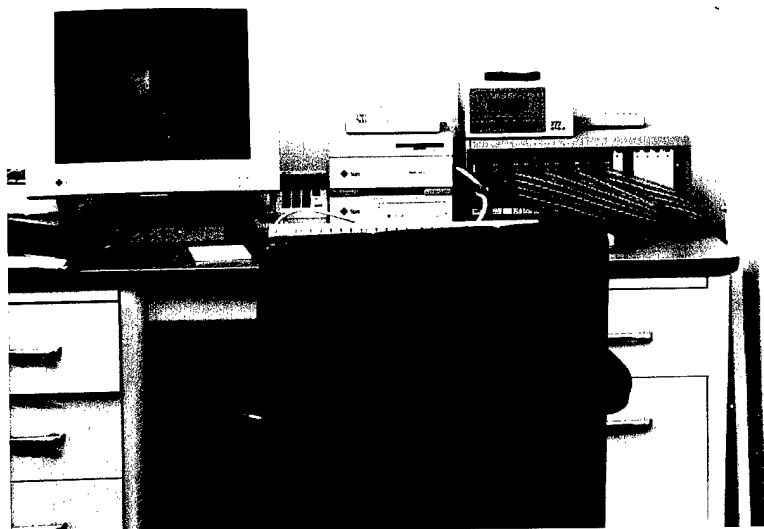
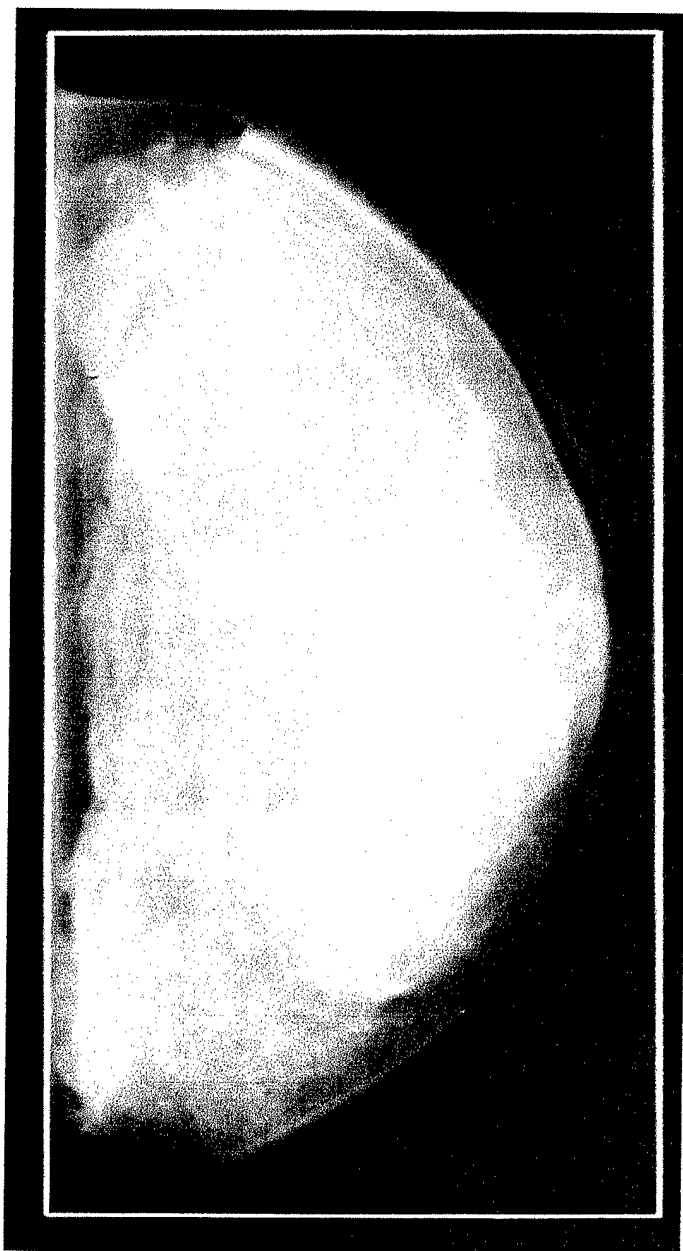Figure B-8: Prototype 2-channel DXM-1 Gantry

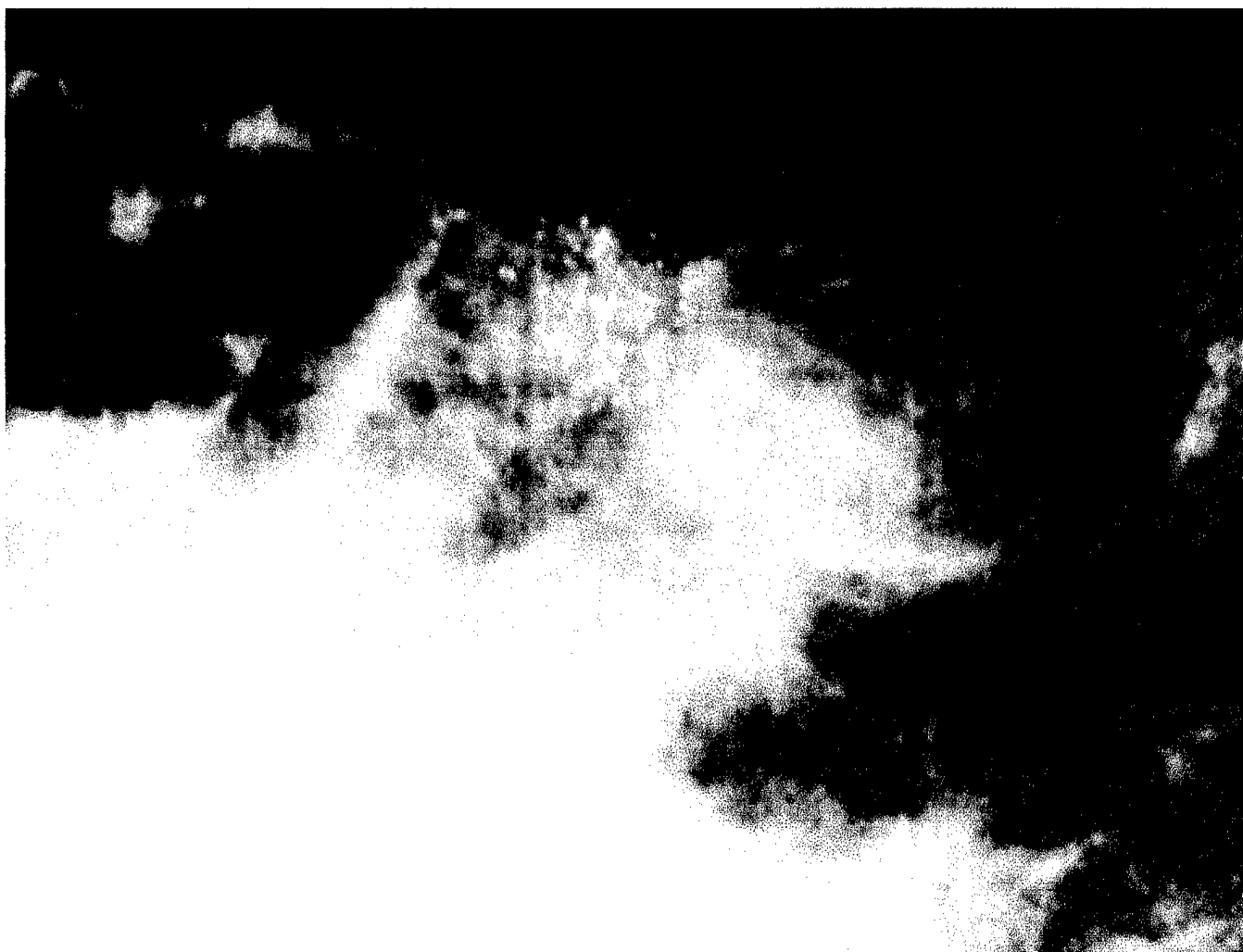Figure B9: Cadaver Breast Image Acquired with the DXM-1

Figure B10: Cadaver Breast Image Acquired with the DXM-1
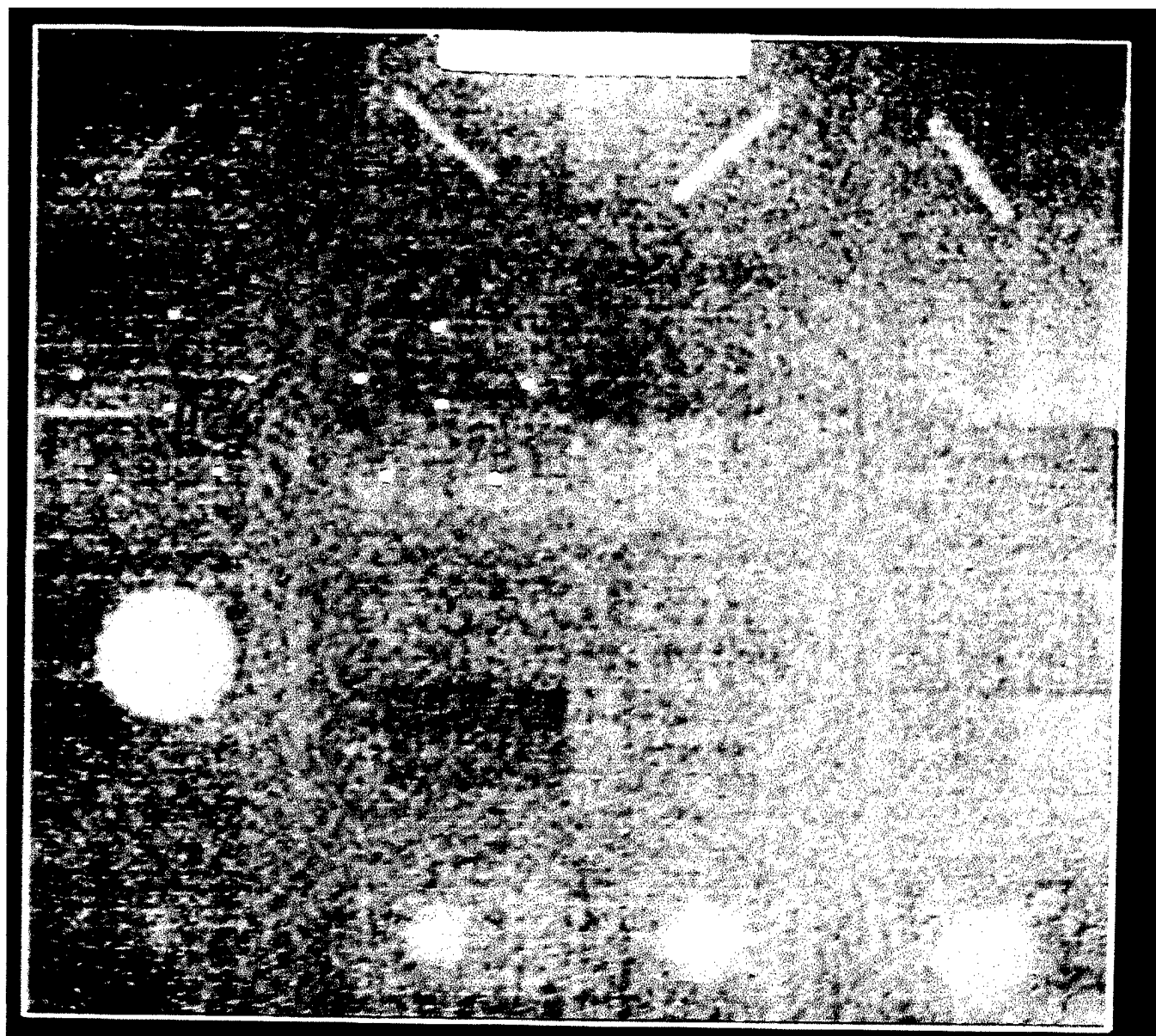Area of Interest Showing Microcalcifications

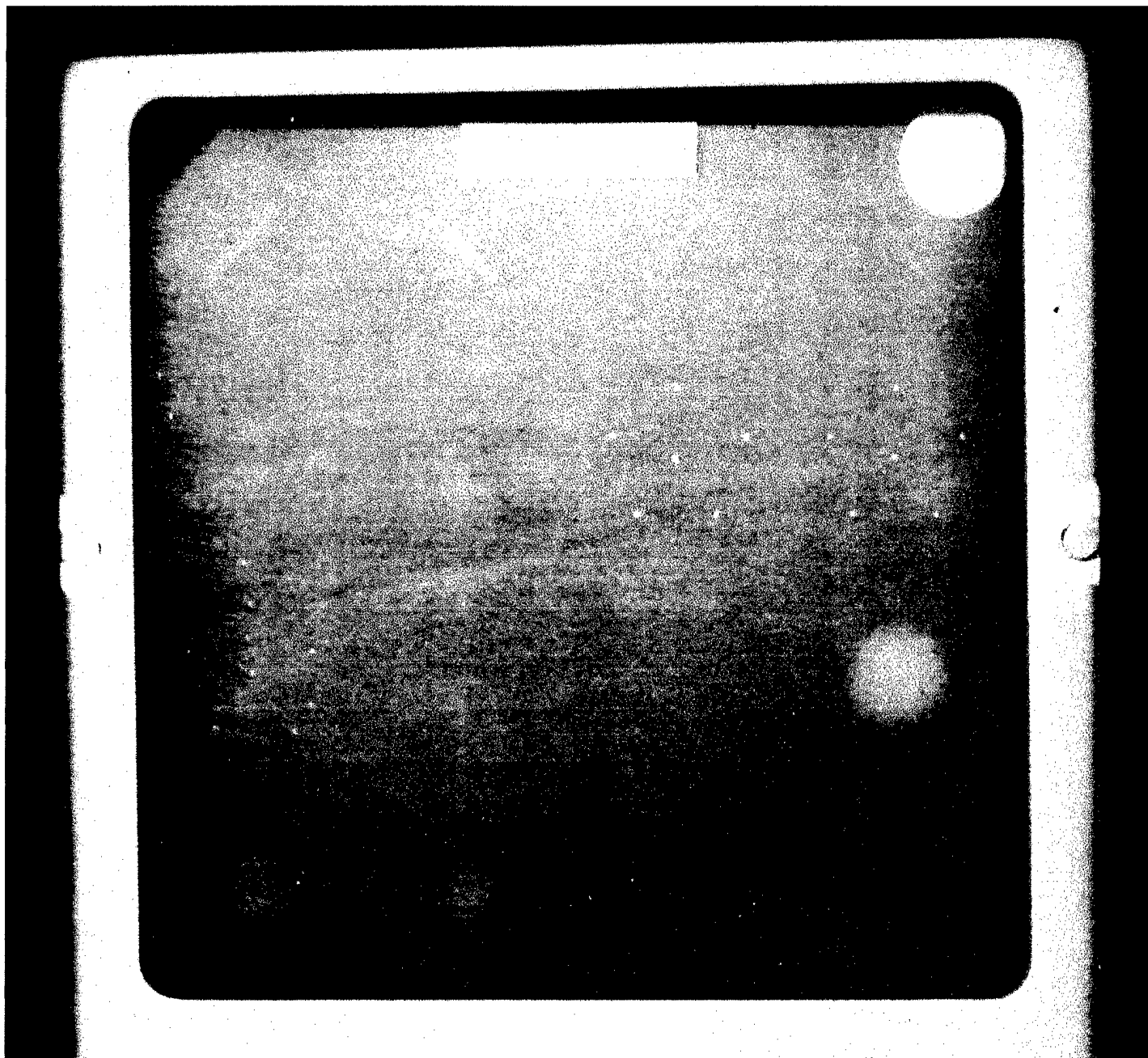Figure B11: ACR Accreditation Phantom Image Acquired with the DXM-1

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Figure B12: ACR Accreditation Phantom Image Acquired with Film/Screen

2. DESCRIPTION

The Mammographic Phantom is made up of a wax block containing 16 various sets of test objects, a 3.3 cm (1.3 inch) thick acrylic base, a tray for placement of the wax block, and a .3 cm (.12 inch) thick cover. All of this together approximates a 4.0 to 4.5 cm compressed breast. Five simulated micro-calcifications, six different size nylon fibers simulate fibrous structures, and five different size tumor-like masses are included in the wax insert.

Figure 2 lists the sizes of the test objects and their position in relation to the notched corner of the wax block.

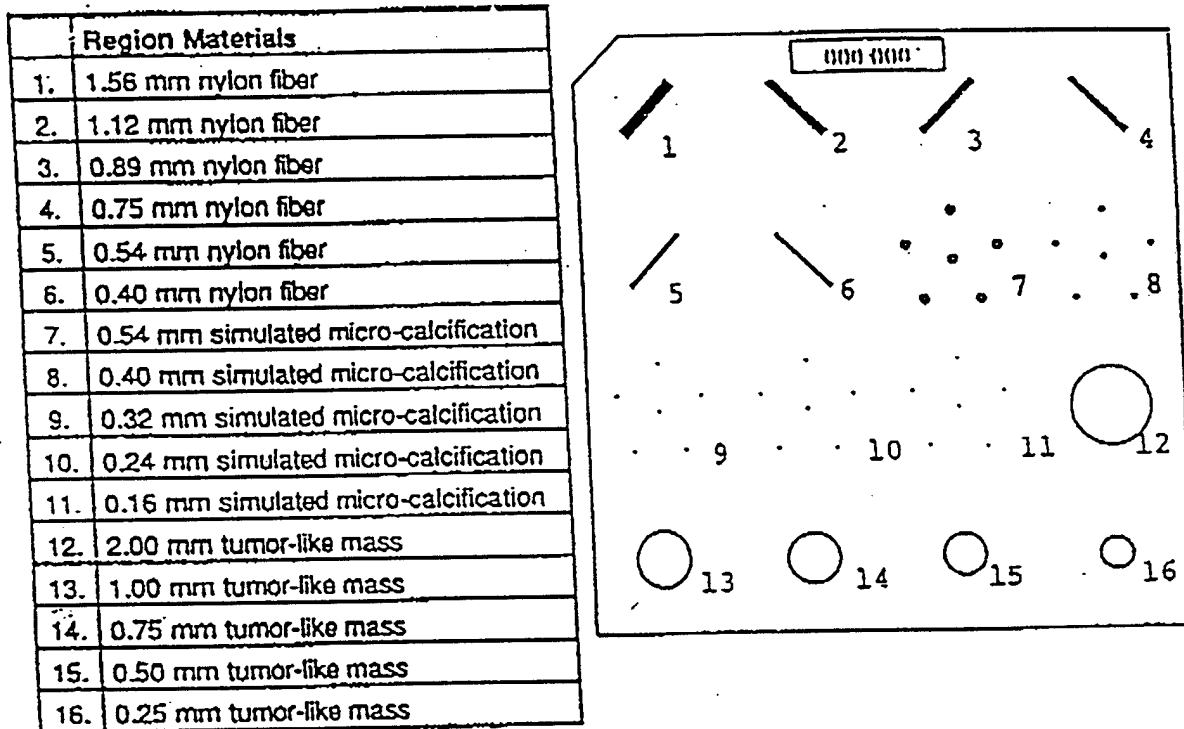|	Region Materials
1.	1.56 mm nylon fiber
2.	1.12 mm nylon fiber
3.	0.89 mm nylon fiber
4.	0.75 mm nylon fiber
5.	0.54 mm nylon fiber
6.	0.40 mm nylon fiber
7.	0.54 mm simulated micro-calcification
8.	0.40 mm simulated micro-calcification
9.	0.32 mm simulated micro-calcification
10.	0.24 mm simulated micro-calcification
11.	0.16 mm simulated micro-calcification
12.	2.00 mm tumor-like mass
13.	1.00 mm tumor-like mass
14.	0.75 mm tumor-like mass
15.	0.50 mm tumor-like mass
16.	0.25 mm tumor-like mass

Figure 2. A schematic view of the Mammographic Phantom giving the test object sizes and position numbers used for reference.

Note: Numbers are for reference only. The wax block can be removed (carefully) and placed in different orientations (even upside down) for a randomized effect if desired.

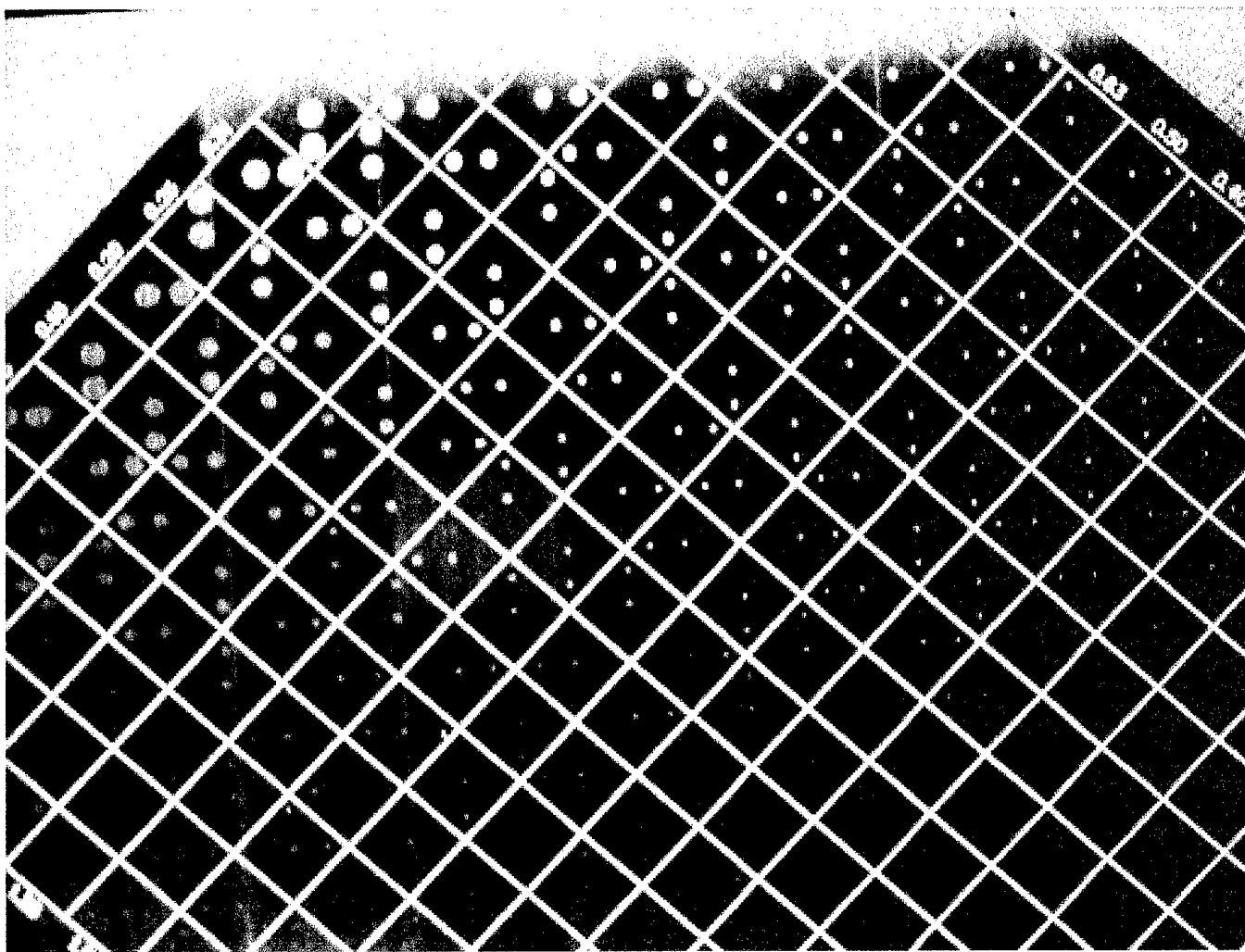Figure B13: ACR Accreditation Phantom Image Schematic

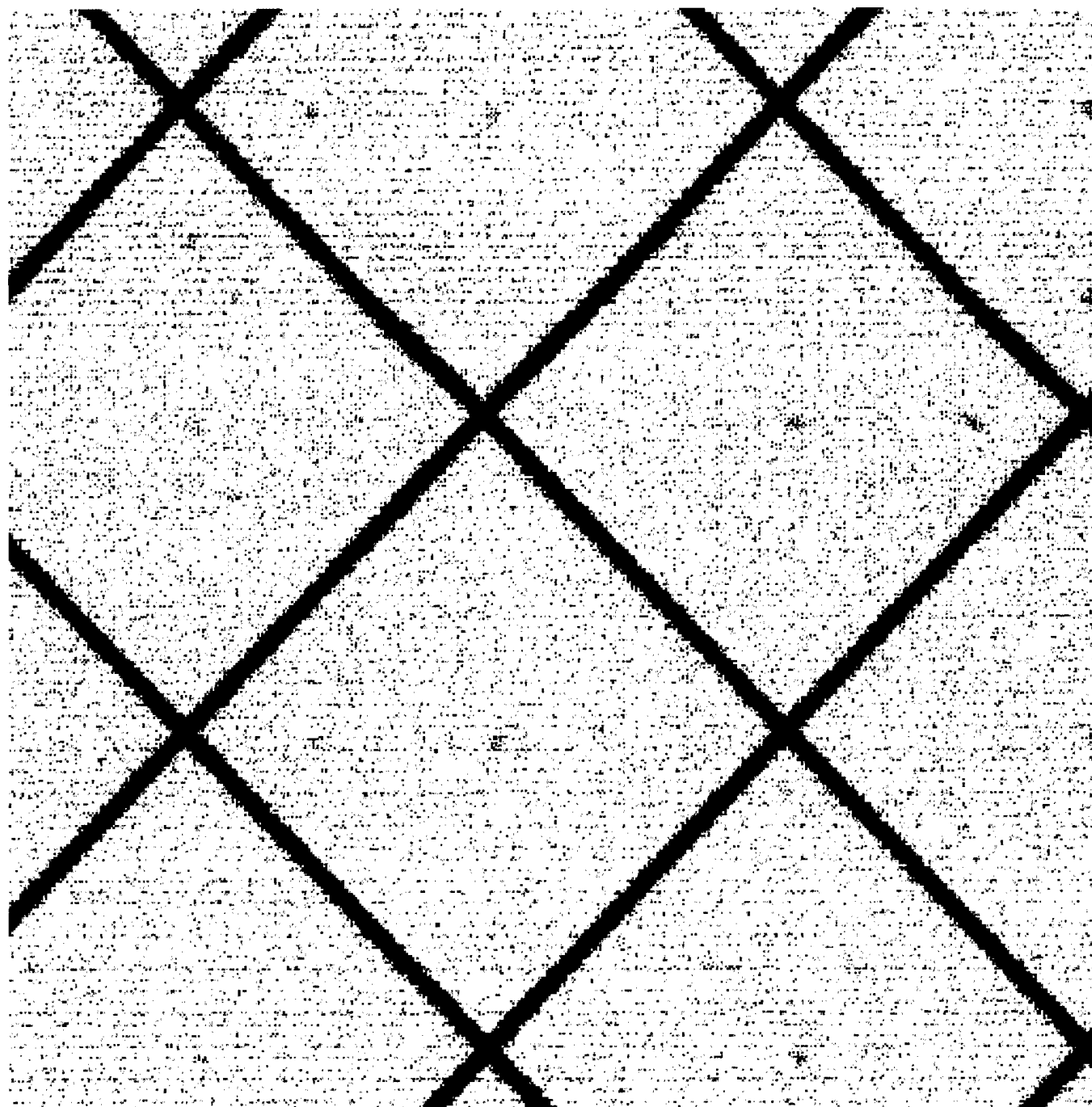Figure B14: CDMAM Phantom Image Acquired with the DXM-1

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Figure B15: CDMAM Phantom Image Acquired with the DXM-1
Area of Interest Showing High Resolution

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